MALARIA

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

The classic symptoms of malaria are high fever with chills, sweats, and headache, which may involve recurrence or intensification of symptoms, especially fever. Depending on the infecting species, fever may appear every other or every third day. Other symptoms may include malaise, nausea, vomiting, diarrhea, cough, arthralgia (joint aches), respiratory distress, and abdominal and back pain. Pallor and jaundice may also be present. Enlargement of the liver and spleen (hepatosplenomegaly) may occur and is more prominent in chronic infections.
Infection with *P. falciparum* is potentially fatal and most commonly manifests as a non-specific febrile illness. Falciparum malaria may present with coagulation defects, shock, renal and liver failure, acute encephalopathy, pulmonary and cerebral edema, and coma. The duration of an untreated primary attack can vary from a week to a month or longer. Relapses of *P. vivax* and *P. ovale* infections can occur at irregular intervals for up to five years. Malaria infections may persist for life (chronic infections), with or without recurrent episodes of fever.

Causative Agent:

There are four *Plasmodium* species (sporozoan parasites) that commonly cause malaria in humans. They are *P.vivax, P. malariae, P. ovale,* and *P. falciparum.*

Differential Diagnosis:

The differential diagnosis can include dengue fever, schistosomiasis, leptospirosis, tick-born fevers, trypanosomiasis, and Yellow Fever.

Laboratory identification:

Malaria is usually diagnosed through a blood smear that can be identified at most reference laboratories. Serology testing is also available, but the test may cross-react with a variety of other illnesses and reliance solely upon serological results for diagnosis may be misleading. PCR testing has limited availability.

> **UPHL:** UPHL does not perform diagnostic testing for malaria, but it will forward thick and thin blood smears to the CDC for testing. The CDC will also perform serologic testing for malaria, but only under special circumstances (e.g., serum of a blood donor suspected of being a source of transfusion-related malaria or serum from laboratories conducting malaria-related studies).

Treatment:

Malaria can be a severe, potentially fatal disease (especially when caused by *Plasmodium falciparum*) and treatment should be initiated as soon as possible.

In endemic areas, the World Health Organization recommends that treatment be started within 24 hours after the first symptoms appear. Treatment of patients with

uncomplicated malaria can be conducted on an ambulatory basis (without hospitalization) but patients with severe malaria should be hospitalized if possible.

In areas where malaria is not endemic, all patients with malaria (uncomplicated or severe) should be kept under clinical observation if possible.

Most drugs used in treatment are active against the parasitic forms in the blood (the form that causes disease) and include:

chloroquine
sulfadoxine-pyrimethamine (Fansidar®)
mefloquine (Lariam®)
atovaquone-proguanil (Malarone®)
quinine
doxycycline

In addition, primaquine is active against the dormant parasite liver forms (hypnozoites) and prevents relapses. Primaquine should not be taken by pregnant women or by people who are deficient in G6PD (glucose-6-phosphate dehydrogenase). Patients should not take primaquine until a screening test has excluded G6PD deficiency.

How to treat a patient with malaria depends on:

The type (species) of the infecting parasite
The area where the infection was acquired and its drug-resistance status
The clinical status of the patient
Any accompanying illness or condition
Pregnancy
Drug allergies, or other medications taken by the patient

Case fatality:

The case fatality rate is 10–40% in the absence of prompt treatment.

Reservoir:

Humans are the only important reservoir of human malaria. Non-human primates are naturally infected by many malarial species that can potentially infect humans, but natural transmission from non-human primates to humans is extremely rare and seldom results in serious disease. The vector for human malaria is the *Anopheles* mosquito, which transmits the parasite from infected human to uninfected human.

Transmission:

Malaria is transmitted by the bite of an infective female *Anopheles* mosquito. Rarely, transmission can be congenital (via the placenta) or can occur through transfusions or the use of contaminated needles.

Susceptibility:

Susceptibility is universal except in humans with specific genetic traits. Tolerance to clinical disease is present in adults in highly endemic communities where exposure is continuous over many years. Persons with sickle cell trait show relatively low parasitemia when infected with *P. falciparum*, and thus are relatively protected from severe disease. Persons infected with HIV are at increased risk of symptomatic falciparum malaria and its severe manifestations.

Incubation period:

The incubation period is approximately 7–14 days for *P. falciparum*; 8–14 days for *P. vivax* and *P. ovale*; and 7–30 days for *P. malariae*. With some strains of *P. vivax*, mostly from temperate areas, there may be a prolonged incubation period of 8–10 months until clinical illness; incubation periods for *P. ovale* may be even longer. With infections acquired by blood transfusion, the incubation period depends on the number of parasites infused; it is usually short but may be up to two months.

Period of communicability:

Malaria is not directly communicable from person to person, except through congenital transmission; however, during parasitemia, the disease may be transmitted to other persons through blood transfusion or through shared, contaminated needles. Infected human hosts can be a source of infection for *Anopheles* mosquitoes for prolonged periods of time (1–3 years or longer, depending on the species of malaria) if not adequately treated.

Epidemiology:

Malaria is endemic throughout the tropical areas of the world. About half of the world's population lives in areas where transmission occurs. Areas with the highest prevalence include sub-Saharan Africa, parts of Central and South America, India, and parts of Oceania and Southeast Asia. Transmission is also possible in more temperate climates, such as in the U.S., if *Anopheles* mosquitoes are present. Locally-acquired cases of malaria have been reported recently in Florida, New York, and Virginia. Mosquitoes in airplanes flying from tropical climates have been the source of occasional cases in persons working or living near international airports. However, nearly all of the malaria cases reported annually in the U.S. (~1000) are acquired outside of the U.S.. *P. vivax* and *P. falciparum* are the most common species worldwide. The worldwide spread of strains of chloroquine-resistant *P. falciparum* and *P. vivax* is of increasing importance. Resistance to other antimalarial drugs is now occurring in many areas where the drugs are widely used.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Identify the source of infection and prevent further transmission.

Prevention:

International Travel

People traveling to malaria-endemic parts of the world should be notified of their risk of contracting the disease and of control measures they can take to protect themselves from mosquitoes. Travelers can use repellents, wear protective clothing, and use mosquito nets when rooms are not screened. They have a choice of medications recommended for prophylaxis depending on circumstances.

Detailed recommendations for preventing malaria are available 24 hours a day from the CDC Malaria Hotline, which can be accessed by telephone at (770) 488-7788, by fax at (888) CDC-FAXX or (888) 232-3299, or on the CDC website at www.cdc.gov/travel.

Travelers and recent immigrants from malaria-endemic regions with symptoms suggestive of malaria should be referred to a health care provider for prompt testing and treatment. Failure to treat individuals with malaria could lead to transmission of the disease to mosquitoes that bite these individuals and then to other people bitten by those mosquitoes.

Chemoprophylaxis:

Non-immune individuals who will be exposed to mosquitoes in malaroius areas must make use of protective measures against mosquito bites and will benefit from the use of suppressive drugs for chemoprophylaxis. The possible side-effects of long-term (up to 3 to 5 months) use of the drug or drug combination recommended for use in any particular area should be weighed against the actual likelihood of being bitten by an infected mosquito.

Vaccine:

No approved vaccine is available yet. Vaccine trials are underway.

Isolation and quarantine requirements:

No restrictions, except for exclusion from blood donation. For blood donation, wait 3 years after completing treatment for malaria; wait 12 months after returning from a trip to an area where malaria is found; and wait 3 years after living in a country or countries where malaria is found.

✓CASE INVESTIGATION

Reporting:

- Report all suspect and confirmed cases of malaria.

Case definition:

Malaria (1995):

Clinical description

Signs and symptoms are variable; however, most patients experience fever. In addition to fever, common associated symptoms include headache, back pain,

chills, sweats, myalgia, nausea, vomiting, diarrhea, and cough. Untreated *Plasmodium falciparum* infection can lead to coma, renal failure, pulmonary edema, and death. The diagnosis of malaria should be considered for any person who has these symptoms and who has traveled to an area in which malaria is endemic. Asymptomatic parasitemia can occur among persons who have been long-term residents of areas in which malaria is endemic.

Laboratory criteria for diagnosis:

Demonstration of malaria parasites in blood films.

Case classification:

Confirmed: an episode of microscopically confirmed malaria parasitemia in any person (symptomatic or asymptomatic) diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country.

Comment:

A subsequent attack experienced by the same person but caused by a different Plasmodium species is counted as an additional case. A subsequent attack experienced by the same person and caused by the same species in the United States may indicate a relapsing infection or treatment failure caused by drug resistance.

Blood smears from questionable cases should be referred to the National Malaria Repository, CDC, for confirmation of the diagnosis.

Cases also are classified according to the following World Health Organization categories:

- *Autochthonous*:
  - *Indigenous*: malaria acquired by mosquito transmission in an area where malaria is a regular occurrence
  - *Introduced*: malaria acquired by mosquito transmission from an imported case in an area where malaria is not a regular occurrence
- *Imported*: malaria acquired outside a specific area (e.g., the United States and its territories)
- *Induced*: malaria acquired through artificial means (e.g., blood transfusion, common syringes, or malariotherapy)
- *Relapsing*: renewed manifestation (i.e., of clinical symptoms and/or parasitemia) of malarial infection that is separated from previous manifestations of the same infection by an interval greater than any interval resulting from the normal periods between attacks.
- *Cryptic*: an isolated case of malaria that cannot be epidemiologically linked to additional cases

Case Investigation Process:

- Fill out morbidity form
- Verify case status.
- Fill out disease investigation form.

- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.

Outbreaks:
One or more non-imported cases of malaria would constitute an outbreak.

Identification of case contacts:
Determine history of previous infection or of possible exposure. If a history of sharing needles is obtained from the patient, investigate and treat all persons who shared the equipment. In transfusion-induced malaria, all donors must be located and their blood examined for malaria parasites and for antimalarial antibodies; parasite-positive donors must receive treatment.

Case contact management:
None

✓REFERENCES

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Red Book: 2003 Report of the Committee on Infectious Diseases (26th Edition), Larry K. Pickering MD, Ed; 2003.

Massachusetts Department of Health Malaria Disease Plan

American Red Cross